Medical Science

To Cite:
Sak N, Hałasiński P, Skowrońska D, Tschuschke M, Lorenz M. Nephrolithiasis - risk factors, prevention, diagnostic and treatment problem of the 21st century - review of the literature. *Medical Science* 2024; 28: e88ms3398
doi: https://doi.org/10.54905/dissi.v28i149.e88ms3398

Authors' Affiliation:
Clinical Department of Gastroenterology, Metabolic, Internal Diseases and Dietetics, University Clinical Hospital in Poznań, 49 Przybyszewskiego, 60-355 Poznań, Poland

*Corresponding Author
Clinical Department of Gastroenterology, Metabolic, Internal Diseases and Dietetics, University Clinical Hospital in Poznań, 49 Przybyszewskiego, 60-355 Poznań,
Poland
Email: natalia.sak@onet.pl

Contact list

Natalia Sak	natalia.sak@onet.pl
Przemysław Hałasiński	przemek0215@gmail.com
Dagmara Skowrońska	dagmara.skowronska@gmail.com
Max Tschuschke	maxtsch@gmail.com
Mikołaj Lorenz	mikolajlorenz@gmail.com

ORCID List

Natalia Sak	0009-0009-3601-3771
Przemysław Hałasiński	0000-0002-7223-3394
Dagmara Skowrońska	0000-0001-7853-1037
Max Tschuschke	0009-0007-9107-808X
Mikołaj Lorenz	0009-0008-6100-0238

Peer-Review History
Received: 05 May 2024
Reviewed & Revised: 09/May/2024 to 22/July/2024
Accepted: 25 July 2024
Published: 30 July 2024

Peer-review Method
External peer-review was done through double-blind method.

Medical Science
pISSN 2321–7359; eISSN 2321–7367

DISCOVERY
SCIENTIFIC SOCIETY

Nephrolithiasis - risk factors, prevention, diagnostic and treatment problem of the 21st century - review of the literature

Natalia Sak*, Przemysław Hałasiński, Dagmara Skowrońska, Max Tschuschke, Mikołaj Lorenz

ABSTRACT

Worldwide, the incidence of kidney stones is increasing rapidly. This relationship is also noticeable with age. Its occurrence is associated with chronic kidney disease. This work aims to present diagnostic processes and prevention in nephrolithiasis. In the search for papers in this review, we based on the PubMed database. The literature we considered was limited to the years 2000-2023, with the use of key words in English: "kidney stones", "kidney stone prevention", "kidney stones kidney stone treatment", "kidney stones risk factors", "kidney stones diagnosis". The research encompassed original, review, and meta-analyses articles. A daily urinalysis is used to provide information about the factors that make up the calculus. In preventing calcium oxalate, cystine, or uric acid stones formation, urine alkalization via a diet rich in fruits and vegetables, vitamin C supplementation, and drinking water are essential. However, the urine should be acidified to prevent the formation of calcium phosphate or struvite stones. Antibiotics, protease inhibitors, and certain diuretics cause the risk of kidney stones. An analogous effect may occur in the case of obesity or weight loss associated with laxative misuse, rapid depletion of muscle tissue, or inadequate hydration. Increasing public awareness of nephrolithiasis and the possible preventive measures can effectively reduce incidents of renal colic attacks. Knowledge of risk factors and increased availability of diagnostics may reduce the incidence of kidney stones.

Keywords: Nephrolithiasis; diagnostic; prevention; risk factors

1. INTRODUCTION

Nephrolithiasis is a common disease with an increasing prevalence of up to 20% worldwide (Kachkoul et al., 2023). The higher prevalence of the disease is due to lifestyle changes, such as lower consumption of vegetables or fruit, higher

consumption of animal proteins, salt, sweetened beverages, and insufficient fluid intake (Sakhaee et al., 2012). Calcareous stones are the most common type of kidney stones and may be associated with hyperoxaluria, hyperuricosuria, cystinuria, or hypercalciuria (Sakhaee et al., 2012). Hypercalciuria has been defined as urinary calcium excretion> 4 mg/kg/day or urinary calcium/creatinine ratio> 0.2. It occurs in less than 60% of patients with recurrent calcium stones (Sakhaee et al., 2012). Hyperoxaluria is an increase in urinary oxalate excretion above 45 mg/day. Hyperoxaluria occurs in 10%-30% of cases of calcium stones.

Hyperoxaluria can also occur after high doses of vitamin C therapy. Calcium oxalate and uric acid stones tend to form in relatively acidic urine (pH <5.5), while calcium phosphate stones precipitate in urine that is alkaline, typically with a pH greater than 7.0 (Prezioso et al., 2015). There is a positive family history of nephrolithiasis in about half of patients with idiopathic nephrolithiasis with hypercalciuria. For these reasons, patients with calcium phosphate stones would need to be assessed for conditions associated with alkaline urine, such as distal renal tubular acidosis (type 1), urinary tract infection and hyperparathyroidism (Sakhaee et al., 2012). Hyperuricosuria is urinary uric acid excretion of uric acid> 750 mg/24 h and accounts for 20%-25% of patients with recurrent calcium stones. Uric acid levels in the blood are within the normal range in more than 80% of these patients.

The incidence of uric acid is increasing due to a higher prevalence of obesity, metabolic syndrome, and a high-purity diet than a defect in uric acid metabolism or reduced uric acid reabsorption. Other risk factors are decreased fluid intake and metabolic acidosis associated with the acidic pH of the urine (Prezioso et al., 2015). Struvite stones occur in patients with recurrent urinary tract infections due to urease-producing organisms such as proteus and klebsiella. Stones can overgrow to form cast stones (Bhat et al., 2018). They consist of magnesium ammonium phosphate and calcium carbonate apatite when ammonia production increases and urine pH is alkaline (Bhat et al., 2018). Cystinuria has been defined as the excretion of cysteine in the urine> 300 mg/day. Cystinuria is a genetic disorder inherited in an autosomal recessive manner with defects in the transport of four amino acids, including cystine, ornithine, arginine, and lysine (Bhat et al., 2018).

Purpose of the work

This paper aims to provide general insights into nephrolithiasis and present the possibilities for diagnosing and preventing kidney stones.

2. REVIEW METHODS

In the search for papers in this review, we based on the PubMed database. The literature we considered was limited to the years 2000-2023, with the use of keywords in English: “kidney stones”, “kidney stone prevention”, ”kidney stones kidney stone treatment”, ”kidney stones risk factors”, ”kidney stones diagnosis”. The research encompassed original, review, and meta-analysis articles.

3. RESULTS AND DISCUSSION

Risk factors

Kidney stone risk factors may often be assessed by urine and blood tests. Urine pH is an essential determinant of kidney stone production. Stones composed of uric acid, cystine, and calcium oxalate typically develop in urine that is acidic in contrast, struvites (magnesium ammonium phosphate) and calcium phosphate stones are prone to develop in urine that is alkaline. Analysis of a 24-hour urine collection could be conducted to examine the presence of calcium, phosphorus, magnesium, uric acid and oxalate to determine stone composition and inhibitory factors for citrate and phytate formation. Increased calcium excretion is another crucial risk factor for the formation of stones and correlates with high dietary acid intake, increased salt intake, and insufficient or excessive vitamin D levels.

Elevated serum calcium levels may indicate primary hyperparathyroidism as the cause of calcium deposition. Kidney stones are a risk factor for chronic kidney disease and can lead to progression to end-stage kidney failure (Siener, 2021). People with kidney stones are more likely to have common risk factors for chronic kidney disease (e.g., hypertension, pre-existing kidney disease, diabetes, proteinuria, albuminuria), as well as atypical factors (e.g., interstitial nephritis, chronic pyelonephritis) (Wagner, 2021). The American Society of Nephrology recommends referring to a nephrologist if the estimated glomerular filtration rate (eGFR) is 60 mL per minute per 1.73 m^2 or lower (stage 3 of chronic kidney disease) or if macroalbuminuria is present (Wagner, 2021) (Table 1).

Table 1 Risk factors of nephrolithiasis.

Category	Risk factors
Dietary	- High intake of animal proteins, salt, sweetened beverages, and vitamin C
	- Low intake of fruits, vegetables, and calcium
Urine Chemistry	- Acidic urine (pH < 5.5) for calcium oxalate, uric acid, and cystine stones
	- Alkaline urine (pH > 7.0) for calcium phosphate and struvite stones
	- High urinary calcium (hypercalciuria), oxalate (hyperoxaluria), uric acid (hyperuricosuria)
Metabolic	- Hypercalciuria, hyperoxaluria, hyperuricosuria, cystinuria
	- Decreased citrate levels in urine (hypocitraturia)
Medical Conditions	-Obesity, metabolic syndrome, diabetes, hypertension, chronic kidney disease, distal renal tubular acidosis
Medications	- Protease inhibitors, antibiotics, diuretics
Hydration	- Low fluid intake, dehydration, high urine osmolality
Genetic	- Positive family history of nephrolithiasis
Others	- Chronic urinary tract infections (for struvite stones), rapid weight loss, laxative abuse

Symptoms

As kidney stones pass through the urinary tract, a distinctive spasm and intermittent pain in the side and abdomen occur. Often, this pain is accompanied by hematuria, vomiting, apathy, or nausea. Fever and chills may also be present. On the other hand, stones in the renal pelvis may not cause symptoms. Differential diagnosis includes infections of the urinary tract or abdominal cavity, as well as musculoskeletal inflammation (Sakhaee et al., 2012).

Diagnostics

Initial examinations in a patient with suspected kidney stones should include urine testing, blood in the urine. If the patient has a fever or has leukocytes in their urine, a urine culture test is crucial in the diagnostic process. Sometimes, the diagnosis is made based on a radiological examination. Stones induced by protease inhibitors and uric acid stones may not be visible on radiography. Ultrasonography or spiral computed tomography (CT) can be detecting all types of kidney stones and is often essential when the diagnosis is uncertain.

Referral to a urologist is justified when there is more than one kidney stone, symptoms worsen with fever, kidney function is impaired, stone transit prolongs, the patient has been diagnosed with hydronephrosis, the patient is pregnant, or the stone has a diameter of more than 5 mm, measured using computed tomography or ultrasonography. The smaller stones pass through the urinary tract spontaneously in 90 % of the patients (Preminger et al., 2007). Urologists increasingly use urethroscopy to remove stones and evaluate urinary tract epithelial lesions. The interstitial deposits that contain calcium oxalates are visible on urethroscopy as a white residue (Preminger et al., 2007).

Prevention of kidney stones

Low dietary calcium intake is a significant risk factor for calcium formation and should be avoided in patients with hypercalciuric stones (Kachkoul et al., 2023). A diet low in calcium increases the absorption of intestinal oxalate and increases its excretion in the urine. A high dietary protein intake increases the daily acid load by producing sulfuric acid from the metabolism of sulfur-containing amino acids (Fontenelle and Sarti, 2019). The production of sulfuric acid and uric acid from protein metabolism increased urinary excretion of uric acid and calcium. It leads to a decrease in the urine pH and the excessive excretion of citrate, which contributes to the formation of stones (Fontenelle and Sarti, 2019). Recommendations suggest reducing protein intake to <1.0 g/kg/day in patients with recurrent stones in treating these patients.

A high salt intake in the diet > 3.0 g / day can promote the formation of stones, thanks to an increase in the excretion of calcium in the urine (Cappuccio et al., 2000). Moreover, low fluid intake, dehydration, and high urine osmolality are significant risk factors for developing kidney stones via increasing calcium and oxalate levels (Cappuccio et al., 2000). Sweetened beverages acidified with

phosphoric acid might increase the risk of calculus development and need to be avoided. Significant dietary intake of vitamin C is also considered a risk factor for calcium oxalate stone formation by increasing urinary oxalate excretion (Ferraro et al., 2016). Low citrate levels in the urine are a significant risk factor for limescale formation. It occurs in about 20%-25% of patients with recurrent nephrolithiasis (Ferraro et al., 2016). Citrate in urine combines with calcium to form a soluble complex.

As a result, less free calcium is available to form calcium oxalate stones (Sakhaee et al., 2012). Hypocitrage is a urinary excretion of citrate <320 mg/day (Ferraro et al., 2016). The primary determinant of citrate excretion in urine is acid-base disorders. Chronic acidosis increases proximal reabsorption in citrate tubules and decreases urinary citrate secretion (Sakhaee et al., 2012). Magnesium is a solid protective inhibitor of limescale formation (Goldfarb et al., 2023). Magnesium-rich foods such as spinach, almonds, yogurt, dark leafy vegetables, and beans are likely to inhibit the formation of calcium crystals (Goldfarb et al., 2023). The problem of kidney stones is not limited to the adult population. The rising incidence of kidney stones in children correlates with the increased prevalence of diabetes, obesity, and hypertension in this demographic group (Sas, 2020).

Because age is a risk factor for kidney stones, adolescents are much more likely to have stones than younger children. Both reasons for the occurrence of stones and the treatment differ in various age groups. Children have a much higher incidence of anatomical and metabolic abnormalities, increased urinary excretion of calcium, and decreased excretion of calcium oxalate and citrate (Sas, 2020). Children affected by cystinuria and other inherited forms of kidney stones are more likely to have a decrease in kidney function compared to the same control age group. However, progression to complete loss of renal function is rare (Sas, 2020). Pregnant women are twice as likely to get calcium phosphate stones compared to women of similar age who are not pregnant.

In these cases, the likelihood of developing calcium phosphate stones is two to three times higher than developing oxalate stones. (Thongprayoon et al., 2021). In the second and third trimesters, the frequency of kidney stones increases. Women have an increased glomerular filtration rate and greater urinary calcium excretion during pregnancy. They may also exhibit a higher urine pH in the second and third trimesters, which can predispose them to calcium phosphate stones. Ultrasound is considered the preferred imaging test for pregnant women. Pregnant women with renal colic have almost twice the risk of preterm birth compared to women who do not have kidney stones (Thongprayoon et al., 2021).

4. CONCLUSIONS

The incidence of kidney stones will increase in the future. They can arise as a result of excessive excretion of calcium, oxalate, uric acid, or cysteine. Urinary pH and elevated urinary calcium excretion are significant risk factors for the formation of kidney stones. Patients with a suspected kidney stone diameter over 5 mm are recommended for referral to a urologist. Strategies to prevent kidney stones include several principles. First of all, low dietary calcium content is a significant risk factor for kidney stones. Secondly, a high dietary intake of protein, vitamin C, and salt contributes to the formation of kidney stones. Dehydration, resulting in high urine osmolality and low levels of citrate in the urine, increases the risk of kidney stones. Magnesium, on the other hand, is a potent antagonist of limescale formation.

Author's Contribution

Natalia Sak: Conceptualization, methodology, investigation
Przemysław Hałasiński: Conceptualization, methodology, investigation
Dagmara Skowrońska: Resources, investigation
Max Tschuschke: Visualization, data curation
Mikołaj Lorenz: Resources, writing- rough preparation

Informed consent

Not applicable.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES

1. Bhat A, Singh V, Bhat M, Kumar V, Bhat A. Spectrum of urinary stone composition in Northwestern Rajasthan using Fourier transform infrared spectroscopy. Indian J Urol 2018; 34(2):144-148. doi: 10.4103/iju.IJU_363_16
2. Cappuccio FP, Kalaitzidis R, Duneclift S, Eastwood JB. Unravelling the links between calcium excretion, salt intake, hypertension, kidney stones and bone metabolism. J Nephrol 2000; 13:169–77.
3. Ferraro PM, Curhan GC, Gambaro G, Taylor EN. Total, Dietary, and Supplemental Vitamin C Intake and Risk of Incident Kidney Stones. Am J Kidney Dis 2016; 67(3):400-7. doi: 10.1053/j.ajkd.2015.09.005
4. Fontenelle LF, Sarti TD. Kidney Stones: Treatment and Prevention. Am Fam Physician 2019; 99(8):490-496.
5. Goldfarb DS, Modersitzki F, Asplin JR, Nazzal L. Effect of a high-citrate beverage on urine chemistry in patients with calcium kidney stones. Urolithiasis 2023; 51(1):96. doi: 10.1007/s00240-023-01468-w. Erratum in: Urolithiasis 2023; 51(1):105. doi: 10.1007/s00240-023-01480-0
6. Kachkoul R, Touimi GB, El Mouhri G, El-Habbani R, Mohim M, Lahrichi A. Urolithiasis: History, epidemiology, aetiologic factors and management. Malays J Pathol 2023; 45(3):333-352.
7. Preminger GM, Tiselius HG, Assimos DG, Alken P, Buck C, Gallucci M, Knoll T, Lingeman JE, Nakada SY, Pearle MS, Sarica K, Türk C, Wolf JS Jr; EAU/AUA Nephrolithiasis Guideline Panel. 2007 guideline for the management of ureteral calculi. J Urol 2007; 178(6):2418-34. doi: 10.1016/j.juro.2007.09.107
8. Prezioso D, Strazzullo P, Lotti T, Bianchi G, Borghi L, Caione P, Carini M, Caudarella R, Ferraro M, Gambaro G, Gelosa M, Guttilla A, Illiano E, Martino M, Meschi T, Messa P, Miano R, Napodano G, Nouvenne A, Rendina D, Rocco F, Rosa M, Sanseverino R, Salerno A, Spatafora S, Tasca A, Ticinesi A, Travaglini F, Trinchieri A, Vespasiani G, Zattoni F. Dietary treatment of urinary risk factors for renal stone formation. A review of CLU Working Group. Arch Ital Urol Androl 2015; 87(2):105-20. doi: 10.4081/aiua.2015.2.105
9. Sakhaee K, Maalouf NM, Sinnott B. Clinical review. Kidney stones 2012: Pathogenesis, diagnosis, and management. J Clin Endocrinol Metab 2012; 97(6):1847–60. doi: 10.1210/jc.2011-3492
10. Sas DJ. Dietary risk factors for urinary stones in children. Curr Opin Pediatr 2020; 32(2):284-287. doi: 10.1097/MOP.0000000000000886
11. Siener R. Nutrition and Kidney Stone Disease. Nutrients 2021; 13(6):1917. doi: 10.3390/nu13061917
12. Thongprayoon C, Vaughan LE, Chewcharat A, Kattah AG, Enders FT, Kumar R, Lieske JC, Pais VM, Garovic VD, Rule AD. Risk of Symptomatic Kidney Stones During and After Pregnancy. Am J Kidney Dis 2021; 78(3):409-417. doi: 10.1053/j.ajkd.2021.01.008
13. Wagner CA. Etiopathogenic factors of urolithiasis. Arch Esp Urol 2021; 74(1):16-23. English, Spanish.